Docket No.: 1322-036

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Lawrence Solomon et al.

Group Art Unit:

Serial No.: 10/598,344

Examiner: Trevor Love

Filed: August 24, 2006

For: SCORED PHARMACEUTICAL TABLETS COMPRISING A PLURALITY OF SEGMENTS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Elliot F. Hahn, Ph.D., declare that I am the Declarant. I am familiar with the invention described in the above identified application and the following tests have been carried out at my direction to evaluate the accuracy of splitting tablets made according to the invention and to compare results obtained from a study that evaluated the accuracy of the splitting of scored tablets of commercially obtained Coumadin®, Lanoxin® and Toprol XL® tablets.

Bi-layer tablets according to the invention disclosed in the above identified application were manufactured in a bi-layer tablet press utilizing tooling that bisected an oval shaped tablet with a score having a 1.14mm score depth. Two distinct color placebo formulas for the bi-layer tablets were used, white placebo for the first scored layer and a colored placebo for the second (un-scored) layer. The tablets were sampled during the compression process and the following test data were obtained:

Bi-layer tablet, average weight (g)	0.58347 g
Bi-layer tablet, average thickness (mm)	3.392 mm
Bi-layer tablet, average hardness (kp)	13.41 kp
First layer, average weight (g)	0.22770 g

First layer, average thickness (mm)	1.309 mm
First layer score penetration depth (%)	87 %

20 tablets were used in the tablet splitting study. Each tablet was weighed in a precision mass balance and the weight of the whole tablet (WT) was documented in grams. One attempt was made to split each tablet into halves. Each tablet was split by hand through the score.

The tablet halves or the two largest tablet fragments (TF) were weighed individually and the individual weights were recorded in grams. The TF weights were compared to the ideal half tablet weight (IHW) defined as 50% of the intact WT weight, in order to quantify the tablet splitting accuracy.

The following chart shows the distribution of the deviation of the weights of the split tablets, made according to the above identified application from the IHW. All of deviations of the TF weights are below 3.5%, where 63% deviate by 2.5% or less and 18% deviate 1.5% or less.

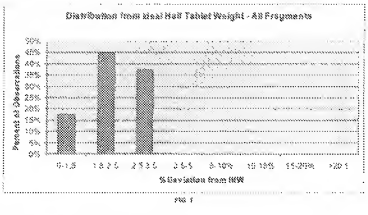

FIG. 1

In a study sponsored by Accu-Break Pharmaceuticals, Inc. the owner of the above identified application that was titled "Accuracy and ease of splitting scored Coumadin, Lanoxin and Toprol XL Tablets" presented at the American Association of Pharmaceutical Scientists (AAPS) conference (November 2009) eighteen volunteers from an outpatient cardiology clinic attempted to manually split 5 tablets each (total 90 tablets per drug) of Coumadin 5mg, Lanoxin 0.125 and Toprol XL 50mg.

Each whole tablet was weighed on a precision mass balance and, after splitting, the resulting halves or the 2 largest tablet fragments (TF) were weighed. The TF weights were compared to the ideal half tablet weight (IHW), or 50% of the whole tablet weight.

The following charts show the comparison of TF deviation from IHW between tablets made according to the present application and scored Coumadin, Lanoxin and Toprol XL respectively. In some cases volunteers were not able to split the tablets, only data from split tablets is considered in this comparison, which range between 35 and 88 tablets (or 70 and 176 TF).

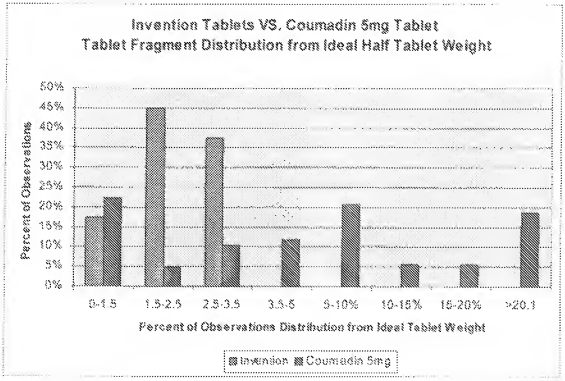

FIG. 2

- All of the TF of the tablets made according to the invention described in the above identified application show a weight that deviates by 3.5% or less while only 38% of Coumadin tablets fall in this range.
- The majority (63%) of Coumadin TF deviate from IHW by 3.5% or more, where 30% deviate more than 10%, 24% more than 15% and 19% more than 20%.

- On average, the deviation of scored Coumadin 5mg TF from IHW was 10% with a standard deviation of 12%. For tablets made according to the above identified application the average TF deviation from IHW was 2.28% with a low standard deviation of 0.7%.
- A low standard deviation indicates that the deviations tend to be very close to the average (or mean), whereas a high standard deviation indicates that the deviations are spread out over a larger range. The high variability in deviation from IHW could pose a risk to patients, particularly in the case of Coumadin which requires careful monitoring and dose precision.

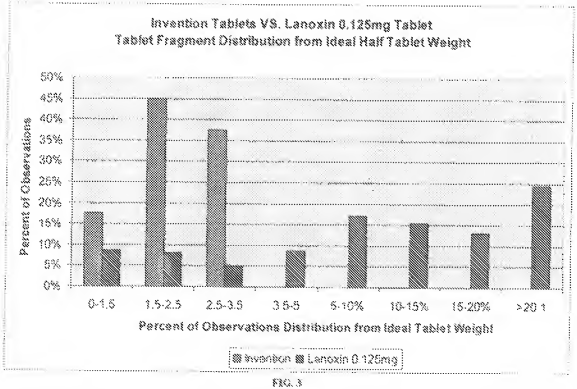

FIG. 3

- All of the TF of the tablets made according to the invention described in the above identified application deviate by 3.5% or less while only 22% of Lanoxin tablets fall in this range.
- The majority (78%) of Lanoxin TF deviate from IHW by 3.5% or more, where 53% deviate more than 10%, 38% more than 15% and 24% more than 20%.

- On average, the deviation of scored Lanoxin 0.125mg TF from IHW was 16% with a standard deviation of 17%. Like in the case of Coumadin 5mg TF deviations from IHW spread out over a large range.

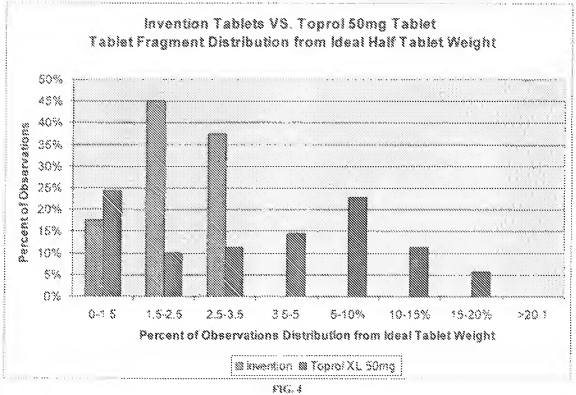

FIG. 4

- All of the TF of the tablets made according to the invention described in the above identified application deviate by 3.5% or less while 46% of Toprol tablets fall in this range
- 54% of Toprol XL TF deviated from IHW by 3.5% or more, where 40% deviate more than 5% from IHW, 17% more than 10% and 6% more than 15%.
- On average, the deviation of scored Toprol XL 50mg TF from IHW was 5.4% with a standard deviation of 5%.
- Of the three scored products compared to tablets made according to the above identified application, Toprol has the least TF variation from IHW, however 55 of 90 tablets attempted to be split were considered unbreakable, or unable to break after one attempt (61% of tablets). Therefore patients requiring to split these

tablets would find difficulty in doing so, whereas all of the tablets made according to the above identified application, split on first attempt.

Variations in weight of the tablet fragments should be interpreted as variations in the dose taken by the patient, which may be clinically relevant, especially for Narrow Therapeutic Index drugs (such as Coumadin or Warfarin) where accurate dosing is particularly important and large variations or deviations are hazardous.

The bi-layer tablets made according to the invention described in the above identified application may be accurately split whereas three typical commercially available monolayer tablets are do not consistently provide accurately split half tablets.

In addition to accuracy in weight of the resulting halves, because the dose in an Accu-B tablet is contained in a pre-divided scored layer and the break occurs through a layer containing no drug, the small deviation seen (3.5% or less, 2.28% in average) occurs within the break layer containing no drug. Therefore the resulting dose does not necessarily carry the weight variation as opposed to conventional products, where the break occurs through the active tablet.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application and of any patent issued thereon.

Dated: Nov 24, 2010

Elliot F. Hahn, Ph.D.